dihydroxyvitamin D_2 (1,24-$[OH]_2D_2$) on cellular growth inhibition and differentiation induction in the androgen-sensitive human prostate cancer cell line LNCaP. Study results revealed that, in the presence of androgen, 1,24-$(OH)_2D_2$ significantly inhibited the growth of LNCaP cells in a manner that was comparable to vitamin D. Furthermore, 1,24-$(OH)_2D_2$ was more potent than vitamin D at inducing PSA release from LNCaP cells, suggesting that it may be a more potent differentiating agent. The authors concluded that, with its lower calcemic toxicity compared with vitamin D, 1,24-$(OH)_2D_2$ may provide a promising vitamin D–based therapeutic modality for prostate cancer. However, before this can be confirmed, the antiproliferative properties of 1,24-$(OH)_2D_2$ need to be demonstrated in an animal model of prostate cancer (in vivo studies) and subsequently in clinical trials.

In summary, although daily oral administration of vitamin D can inhibit prostate cancer growth, the resultant hypercalcemia precludes regular use of this regimen. Weekly administration has been considered but does not appear to be efficacious. Vitamin D analogs that have less hypercalcemic toxicity may prove to be of benefit in the treatment of prostate cancer. However, it is too early to confirm this. ■

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Finasteride and Prostate Cancer

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[*Rev Urol*. 2004;6(2):97-98]

Although testosterone is the major circulating androgen in men, dihydrotestosterone (DHT) is more potent and is the major form of androgen found within the prostate gland.[1] DHT, which is responsible for maintaining prostate growth, is produced through reduction of testosterone by an enzyme called 5-α-reductase.[1] DHT is regarded as an extremely important factor in the pathogenesis of benign prostatic hyperplasia (BPH).[2]

There are 2 isoforms of 5-α-reductase (types 1 and 2). The type 2 enzyme predominates within the prostate and is localized to the fibromuscular stromal compartment.[3] Therefore, finasteride, a selective competitive inhibitor of 5-α-reductase type 2, was developed to address the management of BPH.[4] Accordingly, use of finasteride significantly reduces urinary symptom score, improves urinary flow rates, and reduces prostate volume in men with BPH.[2]

Like BPH, prostate cancer is known to be androgen-dependent, and finasteride inhibits the proliferation of prostate cancer cell lines both in vitro and in vivo.[5,6] These findings incited the National Cancer Institute (NCI) and the South West Oncology Group (SWOG) to consider whether finasteride could reduce the risk of prostate cancer. In 1993, a large-scale study of prostate adenocarcinoma chemoprevention with finasteride was initiated: the Prostate Cancer Prevention Trial (PCPT). A recently published paper reports the findings of this important study.

The Influence of Finasteride on the Development of Prostate Cancer

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N Engl J Med. 2003;349:215-224.

Between January 1994 and May 1997, 18,882 men aged 55 years or older with a normal digital rectal examination (DRE) and a serum prostate-specific antigen (PSA) level of 3.0 ng/mL or lower were randomized to receive either finasteride (5 mg/d) or placebo for 7 years. Prostate biopsy was recommended if the annual serum PSA level, adjusted for the effect of finasteride, exceeded 4.0 ng/mL or if DRE was abnormal. In addition, all men were to be offered an end-of-study biopsy. The authors anticipated that 60% of the participants would have prostate cancer diagnosed during the study or would undergo biopsy at the end of the study. The

primary end point was the prevalence of prostate cancer during the study period.

Approximately 15 months before its anticipated completion, the data and safety monitoring committee recommended early termination of the PCPT because the study objectives had been met and the conclusions were extremely unlikely to change with additional diagnoses of prostate cancer. The rate of diagnosis of prostate cancer or end-of-study biopsy was significantly lower in the finasteride group than in the placebo group (59.6% vs 63.0%; $P < .001$). The results, based on the 86.3% of men (9060) who had completed the 7-year study, revealed that prostate cancer was detected in 803 (18.4%) of 4368 subjects in the finasteride group and 1147 (24.4%) of 4692 in the placebo group, a relative risk reduction of 24.8% (95% confidence interval, 18.6%-30.6%; $P < .001$). However, tumors of Gleason scores 7 through 10 were more common in the finasteride group than in the placebo group (280 [37%] of 757 tumors vs 237 [22.2%] of 1068 tumors [$P < .001$] or 6.4% vs 5.1% [$P < .005$] of the 4368 and 4692 men in the finasteride and placebo groups included in the final analysis, respectively). Sexual side effects were significantly ($P < .001$) more common (though not unexpected) in the finasteride group compared with the placebo group: reduced ejaculate volume (60.4% vs 47.3%), erectile dysfunction (67.4% vs 61.5%), loss of libido (65.4% vs 59.6%), and gynecomastia (4.5% vs 2.8%). Conversely, urinary symptoms were significantly ($P < .001$) more common in the placebo group: increased urinary frequency or urgency (15.6% vs 12.9%), urinary incontinence (2.2% vs 1.9%), and urinary retention (6.3% vs 4.2%). The authors concluded that finasteride prevents or delays the appearance of prostate cancer. However, they also stated that this possible benefit and a reduced risk of urinary problems must be weighed against sexual side effects and the increased risk of high-grade prostate cancer at presentation.

Despite the slight bias toward more men in the finasteride group than in the placebo group receiving an end-of-study biopsy (3820 [40.4%] of 9459 vs 3652 [38.8%] of 9423), demonstrating more cancers being detected in the placebo group than in the finasteride group (576 [15.1%] of 3820 vs 368 [10.1%] of 3652), this study revealed that finasteride exhibits chemopreventative properties. However, finasteride was associated with a significantly ($P < .001$) greater risk of harboring higher Gleason score disease and an increased incidence of sexual side effects compared with placebo.

Men who present with symptoms of BPH should continue to be considered for finasteride therapy and be counseled on the associated risks. In addition, doubling of the serum PSA values for men receiving finasteride has been questioned. A total of 222 subjects who received a recommendation for biopsy would not have received this recommendation if doubling, instead of a factor of 2.3, of the PSA value was used. Sixty-nine of these subjects accepted the recommendation, and prostate cancer was detected in 17. If doubling of the PSA value been used, only 2% of the cancer cases in the finasteride group would have been missed. Therefore, when evaluating the true serum PSA levels in men receiving finasteride, we should consider multiplying the values by at least 2. ■

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Urethral Stents

Overview of Biodegradable Urethral Stents

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[*Rev Urol.* 2004;6(2):98-99]

Biodegradable Urethral Stents

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BJU Int. 2003;92:843-850.

Over the past decade, the development and deployment of a biodegradable urethral stent has gradually gained academic acceptance. The polymers of hydroxyl acids have good biocompatibility properties, and it is possible to make stents with different expansion rates and degradation times. For certain urologic conditions, there is an intrinsic advantage to the use of a bioabsorption device, because it eliminates the need for a second operation for stent removal. In this article, Tammela and Talja